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REMARKS

Claims 29-30, 32, 44-61 are currently pending. Claims 46-49, 52-55, 58-61 are withdrawn. Claims 62-64 are added herein. Support for the new claims can be found throughout the specification and claims as originally filed, for example, in Examples 1-3. Now new matter is added.

Objection to the Figures

The Office has objected to the amendment of Figure 2 filed on August 25, 2003 as purportedly introducing new matter. Figure 2 is presently amended to remove the molecular weight standard objected to by the Office. Replacement Figures 2A-2C are enclosed herewith.

Sequence Rule Compliance

The Office has indicated that the application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 as the nucleotide sequences set forth in the Figure 2 legend are not accompanied by sequence identification numbers. The presently incorporated amendments to the specification provide the sequence identification numbers requested by the Office.

Rejections Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 29-30, 32, 44-45, 50-51 and 56-57 stand rejected under 35 U.S.C. § 112, first paragraph, as purportedly not enabled. In determining that the Applicant's arguments set forth in paper No. 24 were unpersuasive in overcoming this rejection, the Office has indicated that:

It is noted that in Northern blot, there is no expression of mRNA of 20P2H8 gene in normal prostate and bladder tissues. Because of the absence of the expression of mRNA of 20P2H8 gene in normal prostate and bladder tissues as shown by Northern blot, one would expect that there would not be any or there would be very little mRNAs of 20P2H8 gene in normal prostate and bladder tissues, as compared to prostate or bladder cancer tissues, using amplification in a PCR, under the same amplification conditions for both normal and cancer tissues. Thus one would not know which method in the claimed invention is reliable, especially in view that it is well known in the art that PCR is routinely used for detecting differential expression of gene.

It seems that the primary concern of the Office in maintaining this rejection is that, based on the purported discrepancy in expression data, none of the expression data pertaining to expression of

the 20P2H8 gene in prostate and bladder tissues can be considered accurate. The Applicants herein attempt to address this exact point.

With regard to Northern expression data for prostate tissue, the Applicants direct the Office's attention to Figure 3B (lane 3) and Figure 3C (lane 1) for normal expression data and Figure 3C (lanes 2-5) for expression data in prostate cancer xenografts. Low level expression in normal prostate tissue is evident in Figure 3B (lane 3) and 3C (lane 1). Higher level expression (versus Figure 3B) in prostate cancer xenografts is evident in Figure 3C (lanes 2-5).

With regard to RT-PCR expression data for prostate tissue, the Applicants direct the Office's attention to Figure 2C (lane 4) for normal expression data and Figure 2A (lanes 3-5) for expression data in prostate cancer xenografts. 20P2H8 expression was present in both normal tissue and prostate cancer xenografts.

With regard to Northern expression data for bladder tissue, the Applicants direct the Office's attention to Figure 8 (lane 1) for normal bladder expression data and Figure 8 (lanes 3, 5, 7-8) for expression data in tumor samples obtained from patients afflicted with bladder cancer. No expression was observed in the bladder tissue isolated from the normal individual. However, high level expression was observed in selected tumor samples.

Finally, with regard to RT-PCR expression data for bladder tissue, the Applicants direct the Office's attention to Figure 6 for expression data in bladder cancer. No RT-PCR expression data for normal bladder tissue is set forth in the figures.

Accordingly, as there does not appear to be a discrepancy in the data, it is not understood why the data provided is considered inaccurate or unreliable by the office. Thus, the Applicants respectfully request withdrawal of this rejection.

Rejection Under 35 U.S.C. § 102(a)

Claims 29-30, 32, 44-45, 50-51 and 56-57 stand rejected under 35 U.S.C. § 102(a) as purportedly anticipated by WO 9938972 for reasons of record. The Office has further indicated that "since no probe is used in the claimed method, detecting the sequence taught by WO 9938972-A2 in colorectal cancer, breast cancer and lung cancer would also detect the claimed sequence, and thus the method taught by WO 9938972-A2 seems to be the same as the claimed method." Paper No. 27, page 7 (emphasis added).

In response, the Applicants wish to briefly discuss various aspects of the current state of the law of “anticipation” as this issue seems particularly pertinent in the present matter.

No doctrine of the patent law is better established than that a prior patent or other publication to be an anticipation must bear within its four corners adequate directions for the practice of the patent invalidated. If the earlier disclosure offers no more than a starting point for further experiments, if its teaching will sometimes succeed and sometimes fail, if it does not inform the art without more how to practice the new invention, it has not correspondingly enriched the store of common knowledge, and it is not an anticipation.

Dewey & Almy Chemical Co. v. Mimex Co., 124 F.2d 986, 989 (2d Cir. 1942) (Hand, L.); see also *Verdegaal Bros., Inc. v. Union Oil Co.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987) (A reference anticipates a patent claim only if it expressly or inherently describes each and every limitation set forth in the patent claim.). Moreover, “[t]o serve as an anticipating reference, the reference must enable that which it is asserted to anticipate.” *Elan Pharmaceuticals v. Mayo*, 68 USPQ2d 1373, 75 (Fed. Cir. 2003) (emphasis added). “The disclosure in an assertedly anticipating reference must be adequate to enable possession of the desired subject matter. It is insufficient to name or describe the desired subject matter, if it cannot be produced without undue experimentation.” *Id* at 1376 (emphasis added).

Inherent anticipation requires that the missing descriptive material is “necessarily present,” not merely probably or possibly present, in the prior art. *In re Robertson*, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citing *Continental Can Co. USA, Inc. v. Monsanto Co.*, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991) (“Inherency . . . may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.” *Id.* (emphasis added)).

The Office relies on *Ex parte Novitski*, 26 USPQ2d 1389 (Bd. Pat. App & Int. 1993), for the assertion that WO 9938972 “comprises the same method steps as currently claimed using the same composition,” and therefore the claimed method is inherently anticipated. *Novitski* dealt with a situation wherein the claimed method described a method of protecting a plant from pathogenic nematodes, which method comprised inoculating the plant with a nematode-inhibiting strain of *P. cepacia*. The cited art reference, Dart, described a method for inoculation of a plant with a specific type of *P. cepacia* due to its anti-fungal properties on plants. The court found that *P. cepacia*

inherently possessed nematode-inhibiting properties, and thus Dart's method inherently protected the inoculated plant from pathogenic nematodes, while also protecting the plant from fungus.

Importantly, Novitski's claimed method involved the same or similar method of inoculation of plants with the same bacteria as Dart. Thus, the starting materials were the same, even though different effects were claimed/described. The mere fact that the plant was inoculated with *P. cepacia* in Novitski's claims rendered the dual effects necessary consequences of the inoculation. Clearly, the facts of *Novitski* are distinguishable from those in the present circumstance. For example, detection of SEQ ID NO:1 expression is not a necessary consequence of the methods disclosed in WO 9938972.

As previously indicated, WO 9938972 does not teach SEQ ID NO:1, nor detection of its expression. Additionally, WO 9938972 does not teach identifying a sample that exhibits dysregulated cellular growth, diagnosing the presence of cancer, or identifying the presence of a neoplasm in a sample by determining and comparing expression of SEQ ID NO:1. The "closest" sequence in WO 9938972 versus SEQ ID NO:1 of the present claims cited by the Office consists of SEQ ID NO: 3624, of which only about 20% of its length has some similarity to only 9% of the ORF of SEQ ID NO:1 (as based on the alignment provided by the Office together with Paper No. 21). There is no indication in WO 9938972 of whether SEQ ID NO:3624 (out of the 5251 sequences set forth in WO 9938972) is a gene or that, if it is, whether it is expressed in any tissues, let alone whether it is upregulated in any cancerous versus normal tissues. More to the point, WO 9938972 does not enable the presently claimed invention as undue experimentation would be necessary to practice the claimed methods. For instance, one of skill in the art would not know whether, if the appropriate steps were performed utilizing the materials provided in WO 9938972, the expression of SEQ ID NO:1 was being detected. Admittedly, given the teachings of and materials provided in WO 9938972, there does not seem to be a way one of skill in the art would be able to determine the expression of SEQ ID NO:1 without undue experimentation. It seems clear to the Applicants that WO 9938972 has not enabled possession of the claimed subject matter.

The Office asserts that detecting SEQ ID NO:3624 of WO 9938972 through the methods purportedly described therein may also detect expression of SEQ ID NO:1 of the present invention. No evidence has been provided for this assertion. Moreover, based on the present facts, it does not

follow that detecting the expression of SEQ ID NO:3624 of WO 9938972 would necessarily detect the expression of SEQ ID NO:1 of the present claims. Even in the hypothetical circumstance proposed by the Office, it seems extremely unlikely that detecting SEQ ID NO:3624 of WO 9938972, even utilizing a C-terminal specific probe (which is incidentally not taught in WO 9938972), would also detect the expression of SEQ ID NO:1 of the present claims with any particularity.

The Office has suggested that the incorporation of a reference to a specific probe useful for detecting expression of SEQ ID NO:1 would overcome the present rejection. The Applicants thank the Office for the suggestion and herein introduce new dependent claims directed to this aspect. However, based on the foregoing, the Applicants respectfully assert that the Office has not sufficiently set forth the case for inherent anticipation of the present claims, even for those claims not containing a limitation to a specific probe. Accordingly, the Applicants respectfully traverse.

Rejection Under 35 U.S.C. § 102(e)

Claims 29-30, 32, 44-45, 50-51 and 56-57 stand rejected under 35 U.S.C. § 102(e) as purportedly anticipated by U.S. Patent No. 6,262,333 (“the ‘333 patent”) for reasons of record. The Office has further indicated that “since no specific probe is used in the claimed method, detecting the sequence taught by 333’ patent in cancer would also detect the claimed sequence, and thus the method taught by 333’ patent seems to be the same as the claimed method.” Paper No. 27, page 8 (emphasis added).

Again the Office relies on *Ex parte Novitski*, 26 USPQ2d 1389 (Bd. Pat. App & Int. 1993), for the assertion that the ‘333 patent “comprises the same method steps as currently claimed using the same composition,” and therefore the claimed method is inherently anticipated. And again, clearly the facts of *Novitski* are distinguishable from those in the present circumstance. For example, detection of SEQ ID NO:1 expression is not a necessary consequence of the methods disclosed in the ‘333 patent.

As previously indicated, the ‘333 patent does not teach SEQ ID NO:1, nor detection of its expression. Additionally, the ‘333 patent does not teach identifying a sample that exhibits dysregulated cellular growth, diagnosing the presence of cancer, or identifying the presence of a neoplasm in a sample by determining and comparing expression of SEQ ID NO:1. The “closest”

sequence in the '333 patent versus SEQ ID NO:1 of the present claims cited by the Office consists of SEQ ID NO: 380, nonconsecutive portions of which have similarity to only 21% of the ORF of SEQ ID NO:1 (as based on the alignment provided by the Office together with Paper No. 21). More to the point, the '333 patent does not enable the presently claimed invention as undue experimentation would be necessary to practice these methods. For instance, one of skill in the art would not know whether, if the appropriate steps were performed utilizing the materials provided in the '333 patent, the expression of SEQ ID NO:1 was being detected. Admittedly, given the teachings of and materials provided in the '333 patent, there does not seem to be a way one of skill in the art would be able to determine the expression of SEQ ID NO:1 with any accuracy without undue experimentation. As such, it seems clear to the Applicants that the '333 patent has not enabled possession of the claimed subject matter.

The Office asserts that detecting SEQ ID NO:380 of the '333 patent through the methods purportedly described therein may also detect expression of SEQ ID NO:1 of the present invention. No evidence has been provided for this assertion. Moreover, based on the present facts, it does not follow that detecting the SEQ ID NO:380 of the '333 patent would necessarily detect expression of SEQ ID NO:1 of the present claims. Even in the hypothetical circumstance proposed by the Office, it seems unlikely that detecting expression of SEQ ID NO:380 of the '333 patent would also detect the expression of SEQ ID NO:1 of the present claims with any particularity.

The Office has suggested that the incorporation of a reference to a specific probe useful for detecting expression of SEQ ID NO:1 would overcome the present rejection. The Applicants thank the Office for the suggestion and herein introduce new dependent claims directed to this aspect. However, based on the foregoing, the Applicants respectfully assert that the Office has not sufficiently set forth the case for inherent anticipation of the present claims, even for those claims not containing a limitation to a specific probe. Accordingly, the Applicants respectfully traverse.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no.511582002100. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: March 17, 2004

Respectfully submitted,

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Expression of 20P2H8 in LAPC xenografts and restricted normal tissues

Fig.2A

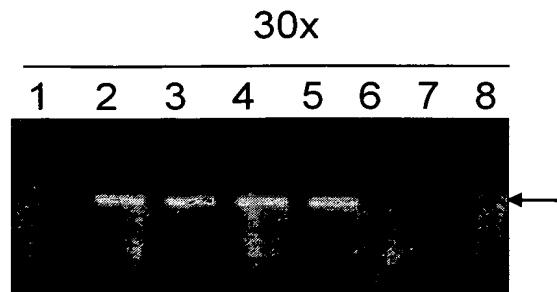


Fig.2B

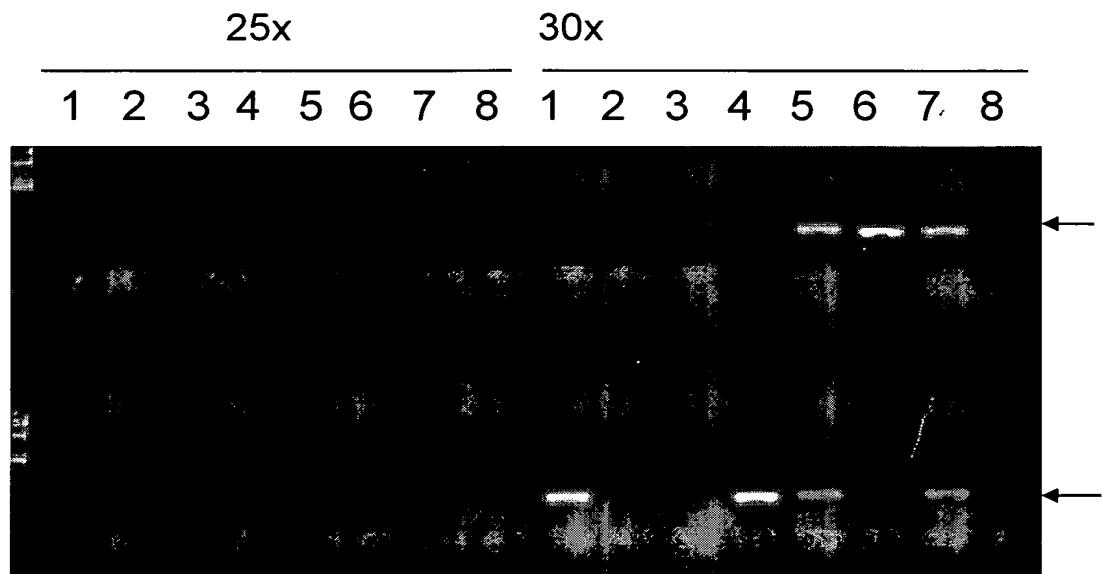


Fig.2C